

REMARKS

Claims 107 and 163-242 are pending. The Brief Description of Figure 1 at page 13 of the specification has been amended to indicate the name and number designations for  $\alpha$ -helical regions of the TEAS structure. Support for these amendments can be found, for example, in U.S. Application Nos. 60/100,993 and 60/130,628, to which the present application claims priority. The specification has been amended at page 26 to delete a reference to helix B. As can be seen from Figure 1 as filed in U.S. Application No. 60/130,628, none of the helices in TEAS were designated as the B helix.

Applicants respectfully request entry of the above amendments. No new matter has been added by these amendments. Attached is a marked-up version of the changes being made by the current amendments.

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The paragraph on page 1, lines 11-13, has been amended as follows:

This work was supported, in part, with funding from NIH (GM54029 and GM07240) and NSF (IBW-9408152) [Federal agencies]. Therefore, the United States Federal Government may have certain rights in the invention.

The paragraph on page 13, lines 5-8 has been amended as follows:

Figure 1. Schematic representation of tobacco 5-epi-aristolochene synthase (TEAS) with bound farnesyl hydroxyphosphonate (FHP), prepared using the RIBBONS software program of Carson, M. and Bugg, C., J. Mol. Graphics 4:121 (1986). Cylinders 1-8 and A represent  $\alpha$ -helices in the NH<sub>2</sub>-terminal domain; cylinders C, D, D1, D2, E, F, G1, G2, H1, H2, H3, I and  $\alpha$ -1 represent  $\alpha$ -helices in the COOH-terminal domain.

The paragraph on page 26, lines 14-23, has been amended as follows:

As exemplified by TEAS, terpene synthases of the present invention can have a first domain segment comprising helices A[, B,] and C (an A-C loop), and a second domain comprising helices J and K (a J-K loop) (Figure 1). The ordering of these loops upon substrate binding results in a closed, solvent-inaccessible active site pocket. As the J-K loop becomes ordered, a lid-type structure is formed that clamps down over the active site entrance in the presence of substrate and an extended aromatic patch deep within the active site pocket is formed. As the A-C loop becomes ordered, it translates inward toward the active site, positioning certain R groups in this loop at or near the active site. Thus, substrate binding to the active site results in a change in protein conformation.